OKUYAMA et al. Appl. No. 10/590,064

Atny. Ref.: 550-850 Amendment

Monday, July 13, 2009

## **AMENDMENTS TO THE CLAIMS:**

Please amend the claims as follows:

1. (Currently Amended) A compound of formula I, or a <u>pharmaceutically</u> phannaceutically acceptable salt thereof,

wherein

Z is  $OR^4$ -or  $NR^1R^2$  wherein each of  $R^1$  and  $R^2$  is independently H, or a hydrocarbyl group;

X-Y is selected from

-C≡C-(CH<sub>2</sub>)<sub>p</sub>-Y

 $-C(R^5)=C(R^6)-(CH_2)_q-Y$ ; and

 $-C(R^5)(R^6)C(R^7)(R^8)-(CH_2)_r-Y;$ 

wherein each of  $R^5$ ,  $R^6$ ,  $R^7$ , and  $R^8$  is independently H or alkyl, and each of p, q and r is independently 2, 3, or 4

X is an alkylene, alkenylene, or alkynylene group, each of which may be optionally substituted by one or more substituents selected from alkyl, COOH, CO<sub>2</sub>-alkyl, akenyl, CN, NH<sub>2</sub>, hydroxy, halo, alkoxy, CF<sub>3</sub>, and nitro;

Y is a polar functional group selected from OH, NO<sub>2</sub>, CN, COR.<sup>3</sup>, COOR<sup>3</sup>, NR<sup>3</sup>R<sup>4</sup>,

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CONR<sup>3</sup>R<sup>4</sup>, SO<sub>3</sub>H, <u>SO<sub>2</sub>-R<sup>3</sup>SO<sub>2</sub>-R</u>3, SO<sub>2</sub>NR<sup>3</sup>R<sup>4</sup> and CF<sub>3</sub>, where each of R<sup>3</sup> and R<sup>4</sup> is independently H or a hydrocarbyl group;

A is phenyl-or pyridyl; and

B is  $(CH_2)_n$  where n is 0;

with the proviso that:

- (i) when A is phenyl, and Z is OH, X-Y is other than C=C-(CH<sub>2</sub>)<sub>2</sub>OH, C=C-(CH<sub>2</sub>)<sub>2</sub>OH, C=C-(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>Me, (CH<sub>2</sub>)<sub>4</sub>CO<sub>2</sub>H; and
- (ii) when A is phenyl, and Z is OMe, X-Y is other than C≡C-(CH<sub>2</sub>)<sub>4</sub>OH; -(CH<sub>2</sub>)<sub>4</sub>-CHO, cis-CH=CH-(CH<sub>2</sub>)<sub>3</sub>OH, trans-CH=CH-(CH<sub>2</sub>)<sub>3</sub>OH;

and wherein the compound is other <u>than thann</u> 1-(N-octylcarbamoyl)methyl-3-carboxmidopyridinuim chloride, 3 -methylcarbamoyl-1-dodecyloxycarbonylmethyl-pyridinium or 6-aminomethylpyridine-2-carboxylic acid ethyl ester.

- 2. (Currently Amended) A compound according to claim 1 wherein Y is selected from [[ON]]CN, OH, COOR<sup>3</sup>, SO<sub>2</sub>NR<sup>3</sup>R<sup>4</sup>, CONR<sup>3</sup>R<sup>4</sup>, where each of R<sup>3</sup> and R<sup>4</sup> is independently H or a hydrocarbyl group.
- 3. (Previously Presented) A compound according to claim 1 wherein each of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> and R<sup>4</sup> is independently H, an alkyl group, an aryl group, or a cycloalkyl group, each of which may be optionally substituted.
- 4. (Previously Presented) A compound according to claim 1 wherein Y is selected from OH, CN, COOR<sup>3</sup>, CONR<sup>3</sup>R<sup>4</sup>, where each of R<sup>3</sup> and R<sup>4</sup> is independently H or an optionally substituted alkyl group.

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5. (Previously Presented) A compound according to claim 1 wherein Y is selected from OH, CN, COOMe, COOH, CONH<sub>2</sub>, CONHMe and CONMe<sub>2</sub>.

Claim 6. (Canceled)

7. (Previously Presented) A compound according to claim 1 wherein X-Y is selected from

-C $\equiv$ C-(CH<sub>2</sub>)<sub>p</sub>-Y; and

-CH=CH-(CH<sub>2</sub>) $_{q}$ -Y;

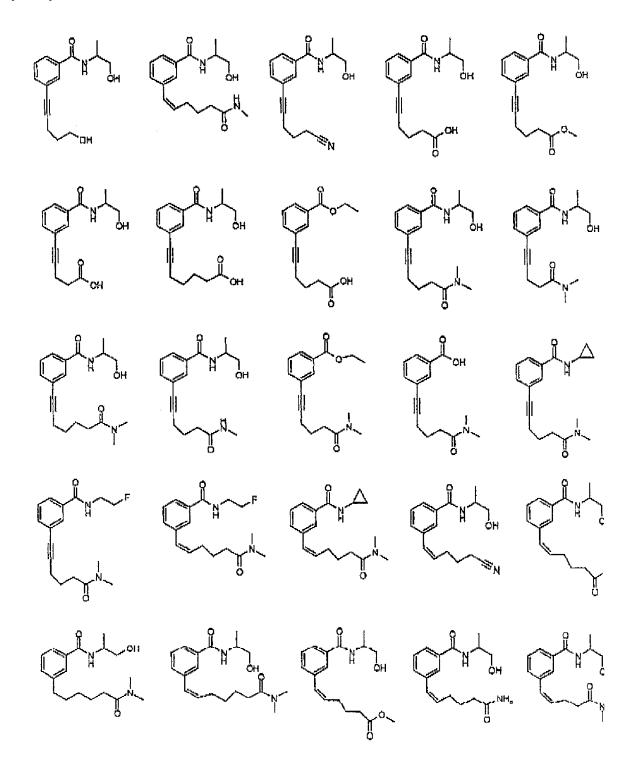
wherein each of p and q is independently 2, 3 or 4.

- 8. (Currently Amended) A compound according to claim [[6]]1 wherein X-Y is cis-C(R<sup>5</sup>)=C(R<sup>6</sup>)-(CH<sub>2</sub>)<sub>q</sub>-Y and q is 2, 3 or 4.
- 9. (Previously Presented) A compound according to claim 1 wherein X-Y is C(Me)<sub>2</sub>-CH<sub>2</sub>-(CH<sub>2</sub>)<sub>r</sub>-Y and r is 2, 3 or 4.
  - 10. (Original) A compound according to claim 1 wherein A is phenyl.
- 11. (Previously Presented) A compound according to claim 1 wherein Z is  $OR^1$  or  $NR^1R_2$  and each of  $R^1$  and  $R^2$  is independently H, an alkyl or a cycloalkyl group, each of which may be optionally substituted by one or more OH or halogen groups.
- 12. (Previously Presented) A compound according to claim 1 wherein Z is selected from OH, OEt, NHCH<sub>2</sub>CH<sub>2</sub>F, NH-cyclopropyl, NHCH(Me)CH<sub>2</sub>OH and NHCH<sub>2</sub>CH<sub>2</sub>OH
- 13. (Previously Presented) A compound according to claim 1 which is selected from the following:

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14. (Original) The compound of claim 13 which is

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- 15. (Original) The compound of claim 14 which is in the form of a racemic mixture.
- 16. (Currently Amended) A method of treating a muscular disorder in a subject in need thereof, said method comprising administering to the subject Use of a compound of formula la, or a pharmaceutically acceptable salt thereof,

wherein

Z is  $OR^1$  or  $NR_1R_2$  wherein each of  $R_1$  and  $R_2$  is independently H, or a hydrocarbyl group;

X is an alkylene, alkenylene, or alkynylene group, each of which may be optionally substituted;

Y is a polar functional group;

A is an aryl or heteroaryl group, each of which may be optionally substituted; and B is  $(CH_2)_n$  where n is 0, 1, 2, 3, 4 or 5;

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in the preparation of a medicament for treating a muscular disorder.

- 17. (Currently Amended) <u>A method [[Use]]</u> according to claim 16 wherein the muscular disorder is a neuromuscular disorder.
- 18. (Withdrawn Currently Amended) A method of treating spasticity and tremors in a subject in need thereof, said method comprising administering to the subject Use of a compound of formula Ia, or a pharmaceutically acceptable salt thereof,

wherein

Z is OR<sup>1</sup> or NR<sup>1</sup>R<sup>2</sup> wherein each of R<sup>1</sup> and R<sup>2</sup> is independently H, or a hydrocarbyl group;

X is an alkylene, alkenylene, or alkynylene group, each of which may be optionally substituted;

Y is a polar functional group;

A is an aryl or heteroaryl group, each of which maybe optionally substituted; and B is  $(CH_2)_n$  where n is 0, 1, 2, 3, 4 or 5;

in the preparation of a medicament for controlling spasticity and tremors.

19. (Withdrawn – Currently Amended) <u>A method of treating a gastrointestinal</u> disorder in a subject in need thereof, said method comprising administering to the

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<u>subject</u> Use of a compound of formula Ia, or a <u>pharmaceutically</u> <del>pharmaceutically</del> acceptable salt thereof,

wherein

Z is OR1 or NR1R2 wherein each of R1 and R2 is independently H, or a. hydrocarbyl group;

X is an alkylene, alkenylene, or alkynylene group, each of which may be optionally substituted;

Y is a polar functional group;

A is an aryl or heteroaryl group, each of which may be optionally substituted; and B is (CH2)n where n is 0, 1, 2, 3, 4 or 5;

in the preparation of a medicarnent for treating a gastrointestinal disorder.

- 20. (Withdrawn Currently Amended) <u>A method [[Use ]]according to claim 19</u> wherein the gastrointestinal disorder is a gastric ulcer.
- 21. (Withdrawn Currently Amended) <u>A method [[Use ]]according to claim 19</u> wherein the gastrointestinal disorder is Crohn's disease.
- 22. (Withdrawn Currently Amended) <u>A method [[Use ]]according to claim 19</u> wherein the gastrointestinal disorder is secretory diarroehea.

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- 23. (Withdrawn Currently Amended) <u>A method [[Use ]]according to claim 19</u> wherein the gastrointestinal disorder is paralytic ileus.
- 24. (Withdrawn Currently Amended) <u>A method [[Use ]]according to claim 16</u> wherein said modulator selectively modulates peripheral cannabinoid receptors.
- 25. (Withdrawn Currently Amended) <u>A method [[Use ]]</u> according to claim 16 wherein said compound selectively modulates peripheral cannabinoid receptors over central cannabinoid receptors.
- 26. (Withdrawn Currently Amended) <u>A method [[Use ]]according to claim 16</u> wherein the compound binds substantially exclusively to peripheral cannabinoid receptors.
- 27. (Withdrawn Currently Amended) <u>A method [[Use ]]according to claim 16</u> wherein the compound is a cannabinoid receptor agonist.
- 28. (Withdrawn Currently Amended) <u>A method [[Use ]]according to claim 16</u> wherein the compound does not substantially agonise central cannabinoid receptors.
- 29. (Withdrawn Currently Amended) A method [[Use ]]according to claim 16 wherein the compound is substantially excluded from the CNS.
- 30. (Currently Amended) <u>A method [[Use ]]according to claim 16 wherein Y is selected from NO<sub>2</sub>, CN, OR<sup>3</sup>, COR<sup>3</sup>, COOR<sup>3</sup>, NR<sup>3</sup>R<sup>4</sup>, CONR<sup>3</sup>R<sup>4</sup>, SO<sub>3</sub>H, SO<sub>2</sub>-R<sup>3</sup>, SO<sub>2</sub>NR<sup>3</sup>R<sup>4</sup> and CF<sub>3</sub>, where each of R<sup>3</sup> and R<sup>4</sup> NO<sub>2</sub>, CN, OR<sub>3</sub>, COR<sub>3</sub>, COOR<sub>3</sub>, NR<sub>3</sub>R<sub>4</sub>, CONR<sub>3</sub>R<sub>4</sub>, SO<sub>3</sub>H, SO<sub>2</sub>-R<sub>3</sub>, SO<sub>2</sub>NR<sub>3</sub>R<sub>4</sub> and CF<sub>3</sub>, where each of R<sub>3</sub> and R<sub>4</sub> is independently H or a hydrocarbyl group.</u>

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- 31. (Currently Amended) A method [[Use ]]compound according to claim 16 wherein Y is selected from CN, COOR3,  $SO_2NR^3R^4$ ,  $CONR^3R^4$ , where each of  $R^3$  and  $R^4$  is independently H or a hydrocarbyl group.
- 32. (Currently Amended) A method [[Use ]]according to claim 16 wherein the compound is as defined in any one of claims 1-5 and 7-15.
- 33. (Withdrawn) A method of treating a disorder associated with the modulation of peripheral cannabinoid receptors, said method comprising administering to a subject in need thereof, a therapeutically effective amount of a compound according to claim 1.
- 34. (Withdrawn) A method according to claim 33 wherein said disorder is associated with peripheral cannabinoid receptor deactivation.
- 35. (Withdrawn) A method according to claim 33 wherein the compound binds substantially agonise central cannabinoid receptors.
- 36. (Withdrawn) A method according to claim 33 wherein the compound binds substantially exclusively to peripheral cannabinoid receptors.
- 37. (Withdrawn) A method according to any claim 33 wherein the compound is substantially excluded from the CNS.
- 38. (Previously Presented) A pharmaceutical composition comprising a compound according to claim 1, or a pharmaceutically acceptable salt thereof, admixed with pharmaceutically acceptable diluent, excipient or carrier.
- 39. (Withdrawn Currently Amended) An assay method of identifying compounds capable of modulating cannabinoid receptor activity, said method comprising using Use of a compound of formula Ia, or pharmaceutically acceptable salt

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thereof, as defined in claim 16 to identify said compounds in an assay for identifying further compounds capable of modulating cannabinoid receptor activity.

40. (Withdrawn – Currently Amended) <u>The method [[Use ]]according to claim 39</u> wherein the assay is a competitive binding assay.